MAY 30 2008

072178(k) Summary

AtheNA Multi-Lyte HSV 1 & 2 IgG Test System

510(k) 072178

Summary of Safety and Effectivenes

As required by 21 CFR 807.92, the following 510(k) summary is provided:

1 Submitter Information

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Establishment Registration Number: 224236

2 Device Information

Proprietary Name: AtheNA Multi-Lyte HSV 1 & 2 IgG Test System
Classification Name: Herpes Simplex Virus Serological reagents
Class: Class II
CFR: 866.3305

3 Predicate Device Information

Manufacturer: Focus Technologies
Name: HerpeSelect 1 and 2 Immunoblot IgG Test System
Methodology: Immunoblot
510(k) Number: K000238

4 Device Description

The AtheNA Multi-Lyte HSV 1 & 2 IgG Test System is a microparticle immunoassay system intended for the qualitative detection of distict IgG antibody to HSV 1 and/or HSV 2.
The test is a multiplexed immunoassay designed to simultaneously detect and distinguish IgG antibody to HSV 1 and/or 2 using recombinant HSV gG-1 and HSV gG-2 antigens.
The test system is comprised of the AtheNA Multi-Lyte HSV 1 & 2 kit and the Luminex Corp instrument and software.

5 Intended Use

The Zeus Scientific, Inc. AtheNA Multi-Lyte HSV 1 & 2 Test System is intended for the qualitative detection of the absence or presence of IgG class antibody to HSV 1 and HSV 2 in human sera. The test is intended to be used as as an aid in the presumptive diagnosis of diseases caused by exposure to Herpes Simplex Virus 1 and 2 in sexually active adults and expectant mothers. The performance of this assay has not been established for use in a pediatric population, neonates and immunocompromised patients.

6 Summary of Technological Characteristics

The AtheNA Multi-Lyte HSV 1 & 2 IgG test system is a multiplexed, microparticle immunoassay designed to detect IgG class antibodies in human sera to HSV 1 and HSV 2 . The assay involves two incubation steps:

1. Diluted test sera re incubated in a vessel containing a multiplexed mixture of bead suspension. The multiplexed bead suspension contains a mixture of distinguishable sets of polystyrene microspheres. Conjugated to the primary set of microspheres are the HSV 1 and 2 antigens. The bead mix also contains one bead set designed to detect nonspecific antibodies in the patient sample if present and four separate bead sets used for assay calibration. If present in patient sera, antibodies to the HSV 1 and/or HSV 2 antigen will bind to the immobilized antigen on the primary bead set. The microspheres are rinsed to remove non-reactive serum proteins.
2. Phycoerythrin-conjugated goat anti-human IgG (Fc specific) is added to the vessel and the plate is incubated. The conjugate will react with IgG antibody immobilized on the solid phase in step 1. The bead suspension is then analyzed by the AtheNA Multi-Lyte instrument. The bead sets are sorted, identified and the amount of reporter molecule (PE conjugate) is determined for each bead set. Using the *Intra-well Calibration Technology*, internal calibration bead sets are used to evaluate unknown specimens to determine their reactivity to Herpes Simplex virus.

7 Performance Data

Non-Clinical

Establishment and Verification of Cut-off

The cut-off corresponds roughly to the mean plus (X) times the Standard Deviation of a negative population, X being the multiplication factor necessary to optimize the assay results. For HSV 1, 7 is the multiplication factor and for HSV 2, 6 is the multiplication factor used to establish the cut-off.

27 known negative samples, confirmed by a commercially distributed ELISA assay were tested to establish the cut-off. Additionally, a minimum of 5 known positive samples, also confirmed by a commercially distributed ELISA assay were tested. The results of the known positive samples were ascertained to exceed the theoretical cut-off as well as the negative samples were ascertained to fall below the theoretical cut-off.

Linearity

Two positive samples (one each for HSV1 and HSV 2) were tested neat and with two-fold serial dilutions using the AtheNA Multi-Lyte HSV 1 & 2 Test System. Results verify the linearity of the assay cut-off.

Limits of Detection

Three (each) strongly positive samples were serially diluted and tested using the AtheNA Multi-Lyte HSV 1 & 2 test system and a commercially available ELISA test system. Results demonstrate that the AtheNA Multi_lyte HSV 1 & 2 test system has comparable limits of detection to the commercially available ELISA test system.

Interfering Substances

Interfering Substances had been done based on industry standard levels of test concentrations recommended in CLSI EP7-A2. The quantity of analyte in each interfering substance is as follows:

Bilirubin: 1mg/dL (low), 15 mg/dL (high)
Albumin: 3.5 g/dL (low), 5 g/dL (high)
Cholesterol: 150 mg/dL (low), 250 mg/dL (high)
Triglycerides: 150 mg/dL (low), 500 mg/dL (high)
Hemoglobin: 20 g/dL (low), 20 g/dL (high)
Intralipid: 300 mg/dL (low), 750 mg/dL (high)
Three samples each for HSV-1 and HSV-2 were chosen based on their performance on the AtheNA Multi-Lyte test system: positive (HSV-1, 818 AU/mL; HSV-2, 566 AU/mL), borderline (HSV-1, 152 AU/ml; HSV-2, 92 AU/mL) and negative (HSV-1, 62 AU/mL; HSV-2, 34AU/mL). The samples were exposed to the possible interfering substance, tested in duplicate and the mean established. All samples showed less than a 20% change in signal with the exception of the negative HSV-1 sample which exhibited an increase in signal of 33% with the low spike of albumin and an increase in signal of 39% with the high spike of albumin. The negative HSV-2 sample showed a change in signal of 37% with the low spike of albumin and 28% with the high spike of albumin. The negative HSV-2 sample also showed changes in signal with bilirubin, 43% and 52%, albumin, 37% and 28%, hemoglobin, 53% and 52% and intralipids, 52% and 34%, low and high spikes of interfering substances respectively. The change of signal in these negative samples did not change the qualitative outcome in these samples, the results remained negative.

Cross-Reactivity

Studies were performed to assess cross reactivity with the Athena Multi-Lyte HSV 1 & 2 IgG test system using sera that were HSV dual-negative by immunoblot testing and that were sero-positive to Measles, Mumps, EBV VCA, EBNA, Rubella, VZV, ANA, CMV and Syphilis. ELISA and micro-particle immunoassay test systems manufactured by Zeus Scientific, Inc. for commercial distribution were used to determine the sero-positivity of the samples. Ten samples for each possible cross-reactant were tested. This study produced no detectable cross-reactivity with samples containing these various antibodies.

Additionally, monoclonal antibodies from potential cross reactants which may be confused clinically with HSV were tested.

Possible Cross Reactant	Positive Results / Number Samples Tested
Measles	0/10
Mumps	0/10
EBV VCA	0/10
EBNA	0/10
Rubella	0/10
VZV	0/10
ANA	0/10
CMV	0/10
Syphilis	0/10

	AtheNA Multi-Lyte		
Monoclonal Antibody	Qualitative Result	HSV 1 IgG	HSV 2 IgG
GONORRHEA 48075	negative	5	4
MONOBILUNCUS 73502	negative	6	2
BACTEROIDES 73049	negative	17	2
VAGINALIS 73297	negative	4	4
PAPILLOMA 170185	negative	3	4
TRACHOMATIS 170120	negative	5	1
GONORRHEA 197587	negative	0	0
PAPILLOMA 184365	negative	2	5
PAPILLOMA 326333	negative	5	3

Precision/Reproducibility

The study was conducted as outlined in Zeus Scientific, Inc. SOP-0180. Six samples were prepared based on their activity with the AtheNA Multi-Lyte HSV 1 & 2 IgG test system. Two samples selected were clearly negative, two were clearly positive and two were near the assay cut0off. This panel was split into six aliquots and tested at three sites. On each day of testing, each sample was diluted twice and each dilution run in quadruplicate, resulting in eight

results. This was performed for three days at each facility. A summary of this testing and calculations for the mean, standard deviation and CV appear in the following tables:

	Reproducibility HSV 1 IgG				
	Inter/ Intra-assay			Inter-Laboratory	
Sample ID	Index Mean	Intra-assay %CV	Inter-assay %CV	Index Mean	%CV of Lab Means
1	26.3	15.0%	18.2%	26.3	21.8%
2	8.4	39.2%	44.0%	8.4	58.2%
3	144.8	11.9%	15.9%	144.8	16.6%
4	195	11.0%	12.3%	195	15.9%
5	311.8	8.4%	9.9%	311.8	10.7%
6	392.2	8.5%	9.1%	392.2	12.8%

	Reproducibility HSV 2 IgG				
	Inter/ Intra-assay			Inter-Laboratory	
Sample ID	Index Mean	Intra-assay %CV	Inter-assay %CV	Index Mean	%CV of Lab Means
1	16.4	36.4%	36.8%	16.4	44.0%
2	20.8	27.9%	31.0%	20.8	40.0%
3	155.7	15.5%	21.0%	155.7	23.6%
4	114.2	10.6%	13.7%	114.2	18.1%
5	442.3	9.2%	12.4%	442.3	13.9%
6	356.2	8.0%	14.1%	356.2	16.1%

Performance Data

Clinical

Expected Values

For the purpose of determining prevalence in the patient category "Prospectively Collected Samples from Sexually Active Adults", 317 patients whose sera were submitted for determining the absence or presence of HSV 1 & 2 IgG antibodies were tested at three clinical sites:

Age	Sex	HSV 1 Positive	HSV 1 Negative	total	Observed % Prevalence HSV-1	HSV 2 Positive	HSV 2 Negative	total	Observed % Prevalence HSV-2
17-19	Male	4	1		2.1%		5		0.0%
	Female	7	8		3.7%	2	12		2.2%
20-29	Male	20	22		10.6%	6	36		6.7%
	Female	49	39		25.9%	22	66		24.7%
	Sex?	2	4		1.1%	2	4		2.2%
30-39	Male	16	18		8.5%	8	26		9.0%
	Female	31	7		16.4%	12	27		13.5%
	Sex?	1	2		0.5%	1	2		1.1%
40-49	Male	14	6		7.4%	6	14		6.7%
	Female	10	8		5.3%	7	11		7.9%
50-59	Male	19	5		10.1%	12	12		13.5%
	Female	6	3		3.2%	3	6		3.4%
	Sex?	1			0.5%	1			1.1%
60-69	Male	5	2		2.6%	4	3		4.5%
	Female	4	2		2.1%	3	3		3.4%
Sub-total	Male	78	54		41.3%	36	96		40.4%
	Female	107	67		56.6%	49	126		55.1%
	Sex?	4	6		2.1%	4	6		4.5%
	Total	189	127	**317**	59.6%	89	228	**317**	28.1%

Note: HSV-1 total includes one equivocal result

For the purpose of determining prevalence in the patient category "Expectant Mothers", 150 retrospective samples were tested. Fifty samples were from mothers in the first trimester, 50 mothers were in the second trimester and 50 were in the third trimester of pregnancy:

Age	Sex	HSV 1 Positive	HSV 1 Negative	total	Observed % Prevalence HSV-1	HSV 2 Positive	HSV 2 Negative	total	Observed % Prevalence HSV-2
17-19	Female	12	7		12.0%	8	11		13.1%
20-29	Female	52	27		52.0%	37	42		60.7%
30-39	Female	25	8		25.0%	12	21		19.7%
40-49	Female	11	8		11.0%	4	15		6.6%
	Total	100	50	**150**	66.7%	61	89	**150**	40.7%

Agreement Summaries:

Performance in a Population of Sexually Active Adults

Zeus Scientific and two outside investigators assessed the device using a total of 317 prospective samples. The samples were sequentially submitted to the laboratories, archived and masked. The samples were collected from sexually active adults between the ages of 17 and 70 and submitted for Herpes simplex antibody testing.

Sexually Active Adults HSV-1

		Predicate Immunoblot					
		Positive	Indeterminate	Negative	Site Total	Sensitivity/ Specificity	95% CI
AtheNA Multi-Lyte	Site 1						
	Positive	82	1	4	87	96.5% 82/85	90.0% to 99.3%
	Equivocal				0		
	Negative	3		45	48	91.8% 45/49	80.4% to 97.7%
	Site Total	85	1	49	135		
	Site 2						
	Positive	49		2	51	100.0% 49/49	94.1% to 100.0%
	Equivocal		1		1		
	Negative			32	32	91.4% 32/35	77.0% to 98.2%
	Site Total	49	0	35	84		
	Site 3						
	Positive	49		2	51	100.0% 49/49	94.1% to 100.0%
	Equivocal				0		
	Negative			47	47	95.9% 47/49	86.0% to 99.5%
	Site Total	49	0	49	98		
	Combined Sites						
	Positive	180	1	8	189	98.4% 180/183	95.3% to 99.7%
	Equivocal			1	1		
	Negative	3		124	127	92.5% 124/134	86.7% to 96.3%
	Combined Total	183	1	133	317		

Sexually Active Adults HSV-2

		Predicate Immunoblot					
		Positive	Indeterminate	Negative	Site Total	Sensitivity/ Specificity	95% CI
AtheNA Multi-Lyte	Site 1						
	Positive	43		2	45	97.7% 43/44	88.0% to 99.9%
	Equivocal				0		
	Negative	1	1	88	90	97.8% 88/90	92.2% to 99.7%
	Site Total	44	1	90	135		
	Site 2						
	Positive	16		3	19	100% 16/16	82.9% to 100.0%
	Equivocal				0		
	Negative			65	65	95.6% 65/68	87.6% to 99.1%
	Site Total	16	0	68	84		
	Site 3						
	Positive	21		4	25	100.0% 21/21	86.7% to 100.0%
	Equivocal				0		
	Negative			73	73	94.8% 73/77	87.2% to 98.6%
	Site Total	21	0	77	98		
	Combined Sites						
	Positive	80		9	89	97.6% 80/82	91.4% to 99.7%
	Equivocal				0		
	Negative	1	1	226	228	96.2% 226/235	92.9% to 98.2%
	Combined Total	81	1	235	317		

Performance in a Population of Expectant Mothers

Comparative studies were performed at Zeus Scientific using archived, masked sera obtained from a serum vendor. The 150 expectant mothers ranged in age from 18 to 48. Of these 150 expectant mothers, 50 were in their first trimester of pregnancy, 50 were in their second trimester and 50 were in their third trimester of pregnancy.

HSV-1

AtheNA Multi-Lyte	Expectant Mothers: Predicate Immunoblot Results			
	Positive	Indeterminate	Negative	Site Total
positive	98		2	100
equivocal				0
negative			50	50
Site Total	98	0	52	150

Sensitivity = 100.0% 98/98 (95%CI 97.0% to 100.0%)
Specificity = 96.2% 50/52 (95%CI 86.8% to 99.5%)

Confidence intervals calculated using the EXACT method

HSV-2

AtheNA Multi-Lyte	Expectant Mothers: Predicate Immunoblot Results			
	Positive	Indeterminate	Negative	Site Total
positive	59		2	61
equivocal				0
negative			89	89
Site Total	59	0	91	150

Sensitivity = 100.0% 59/59 (95%CI 95.1% to 100.0%)
Specificity = 97.8% 89/91 (95%CI 92.3% to 99.7%)

Confidence intervals calculated using the EXACT method

Agreement with CDC Panel

The following information is from a serum panel obtained from the CDC and tested by Zeus Scientific, Inc. The results are presented to convey further information on the performance of the AtheNA Multi-Lyte HSV 1 & 2 IgG assay with a masked, characterized serum panel. This does not imply endorsement of the assay by the CDC.

HSV-1

AtheNA Multi-Lyte	CDC Panel: Positive	CDC Panel: Indeterminate	CDC Panel: Negative	Site Total
positive	50			50
equivocal				0
negative			50	50
Site Total	50	0	50	100

Pos % Agreement = 100.0% 50/50 (95%CI 94.2% to 100.0%)
Neg % Agreement = 100.0% 50/50 (95%CI 94.2% to 100.0%)

Confidence Intervals calculated using the EXACT method

HSV-2

AtheNA Multi-Lyte	CDC Panel: Positive	CDC Panel: Indeterminate	CDC Panel: Negative	Site Total
positive	48		1	49
equivocal				0
negative			51	51
Site Total	48	0	52	100

Pos % Agreement = 100.0% 48/48 (95%CI 94.0% to 100.0%)
Neg % Agreement = 98.1% 51/52 (95%CI 89.7% to 100.0%)

Confidence Intervals calculated using the EXACT method

Performance in a Low Prevalence Population

The relative specificity of the AtheNA Multi-Lyte HSV 1 & 2 test system was assessed internally using sera from a low prevalence population. The low prevalence population was comprised of sera stored in a serum bank at the manufacturer site. Archived, masked serum samples from 18 and 19 year old subjects previously tested for infections considered non-sexual in nature was tested and performance compared to the predicate device.

HSV-1 Reactivity: The predicate immunoblot device was positive for 7 samples and negative for 60 samples. The AtheNA Multi-Lyte HSV 1& 2 IgG test system agreed with 100.0% (8/8) of immunoblot positives and 96.7% (56/58) of immunoblot negatives.

HSV-2 Reactivity: The predicate immunoblot device was positive for 0 samples and negative for 67 samples. The AtheNA Multi-Lyte HSV 1& 2 IgG test system agreed with 100% (0/0) of immunoblot positives and 100% (67/67) of immunoblot negatives.

HSV-1

AtheNA Multi-Lyte	Low Prevalence Population / Predicate Immunoblot Results: Positive	Indeterminate	Negative	Site Total
positive	8	0	2	10
equivocal	0	0	0	0
negative	0	0	56	56
Site Total	8	0	58	66

Sensitivity = 100.0% 8/8 (95%CI 63.1% to 100.0%)
Specificity = 96.7% 56/58 (95%CI 88.1% to 99.6%)

Confidence Intervals calculated using the EXACT method

HSV-2

AtheNA Multi-Lyte	Low Prevalence Population / Predicate Immunoblot Results: Positive	Indeterminate	Negative	Site Total
positive	3	0	1	4
equivocal	0	0	0	0
negative	0	0	62	62
Site Total	3	0	63	66

Sensitivity = 100.0% 3/3 (95%CI 29.2% to 100.0%)
Specificity = 98.4% 62/63 (95%CI 91.2% to 100.0%)

Confidence Intervals calculated using the EXACT method

NOTE:

The test is for *in vitro* use only.
The performance of this assay has not been established for neonatal, pediatric, immunocompromised populations, cord blood or pre-transplant patients.
The use of whole blood or plasma is not established.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 30 2008

Ms. Ewa Nadolczak
Manager, Clinical Affairs
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200 Evans Way
Branchburg, NJ 08876

Re: K072178
Trade/Device Name: AtheNA Multi-Lyte® HSV 1 & 2 IgG Test System
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes Simplex Virus Serolical Reagents
Regulatory Class: Class II
Product Code: MXJ, MYF
Dated: May 23, 2008
Received: May 28, 2008

Dear Ms. Nadolczak:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): (k) 072178

Device Name: AtheNA Multi-Lyte® HSV 1 & 2 IgG Test System

Indications For Use:

The Zeus Scientific, Inc. AtheNA Multi-Lyte® HSV 1 & 2 IgG Test System is intended for the qualitative detection of the presence or absence of human IgG class antibodies to Herpes Simplex virus I and 2 in human sera. The test is indicated for sexually active adults and expectant mothers, as an aid for presumptively diagnosing Herpes Simplex 1 and 2. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1 and HSV-2. The test is not intended for donor screening or for self testing.
The performance of this assay has not been established for use in a pediatric population, neonates, immunocompromised patients, for use by point of care facilities or for use with automated equipment.

Prescription Use __X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) k072178